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Commentary: The past, present and future of affordable antiretroviral therapy in Africa

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In 2002, the Zambian government took an important decision to provide low cost, antiretroviral triple therapy (ART) to respond to the high burden of disease caused by HIV/AIDS: around one in six of the country's 10.2 million population were HIV positive. To reduce the cost of treatment, the government announced that it would import generic versions of ART from India.[1] At the time there was considerable debate, much of it driven by vested interests, around the safety, efficacy and legality of generic antiretroviral drugs.[2] But with proprietary triple therapy at the time costing more than three times the generic equivalent,[3] the government pressed ahead, noting that they would collect comparative safety and efficacy data.[1]

These comparative data are reported in a study in this months' *IJE*. The study, by Stringer *et al.*,[4] compares outcomes among 14 000 patients who were prescribed generic and proprietary versions of zidovudine-based antiretroviral therapy between 2004 and 2007 in Zambia. The results validate the Zambian government's decision to procure generic antiretrovirals that show comparable survival and immunological response compared with proprietary drugs, and marginally fewer regimen substitutions. It is worth noting that, although these data are reassuring, quality assurance and bioequivalence are the more important regulatory requirements for generic drugs. Bioequivalence means that the bioavailabilty of the originator and the generic drug are essentially the same, so assurance of bioequivalence also provides assurance of efficacy and safety. The Indian generic drugs used by Zambia have been validated according to these criteria, receiving approval by both the WHO Pre-Qualification Programme in 2004 and the US Food and Drugs Administration so called tentative approval of generic ARVs in 2006.

Amid the ever accumulating data describing the clinical and public health benefits of providing ART, it is easy to lose sight of the fact that prior to ART people presenting with AIDS-defining illness in resource-limited settings could only expect to live ~6 months.[5,6] Zambia's decision to respond early to the HIV/AIDS epidemic has undoubtedly saved thousands of lives and has also resulted in a national programme that boasts one of the highest rates of treatment coverage in Africa. As of the end of 2011, ART coverage in Zambia was estimated at 72%, far higher than the average of 48% for low- and middle-income settings, and higher in absolute numbers than any developed country: there are more people on antiretroviral therapy in Zambia (283 863) than the USA (268 000).[7] The country is also notable in having been one of the first in Africa to move towards providing tenofovir as first-line therapy. This policy shift, which was implemented 2 years before it was recommended by the WHO, has subsequently been supported by programme data showing better tolerability.[8] And last year the government continued its tradition of acting ahead of international recommendations by releasing guidance for early initiation ART in serodiscordant couples to reduce HIV transmission, following recent evidence of preventive benefit.[9]

The majority of people on ART in Africa are treated with generic drugs. Widespread access to ART has been demonstrated to yield substantial medical and public health benefits in terms of reduced mortality, morbidity and transmission. In the absence of a cure HIV/AIDS is a chronic disease, yet with effective treatment people with HIV/AIDS in Africa can expect to enjoy a relatively normal life expectancy.[10] And in the absence of an effective vaccine, ART has proven to be the most effective biomedical intervention to prevent HIV transmission.[11]

Yet these benefits will only be guaranteed over the long term if countries are able to continue to improve treatment coverage while at the same time ensuring that those on treatment remain adherent to an effective regimen. The continued availability of affordable, effective ART is central to achieving these goals. However, the political struggle to secure access to affordable medicines is far from over.

As Zambia and other African governments proceed into the second decade of providing ART at scale, the number of people developing resistance to first-line regimens is, as expected, growing. There are also

increasing numbers of reports of patients failing second-line therapy.[12] Unfortunately, the global enforcement of intellectual property protection over the last decade puts into serious question the extent to which countries like Zambia will be able to ensure access to newer regimens.

WHO recommends that countries begin to develop policies to have third-line regimens in place,[13] but currently third-line regimens are widely patented and can cost as much as 19 times the price of first line. Consequently, most African countries make no provision for third-line therapy.[14] Once again, Zambia is an exception, and the latest ART guidelines recommend two drugs—darunavir and raltegravir—for the management of patients failing second line. However, these recommendations are preceded by the sobering caveat that there are currently no third-line options available in the public sector due to the high cost of these drugs.[13] Darunavir and raltegravir have each grossed over $US1 billion in sales but the proprietary companies refuse to provide equitable prices for all low- and middle-income countries.[3]

Ten years ago the high cost of ART meant that HIV/AIDS was a disease that was either treatable or untreatable, depending on whether you lived in the Western world or in Africa. For people failing treatment, there is a risk of returning to this inequitable situation. This will only be avoided by the kind of decisive political action exemplified by Zambia back in 2002 that put the provision of life-saving ART above the intellectual property interests of pharmaceutical companies.

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